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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER
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ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

## Office Action Summary

Application No.

09/537,858

Applicant(s)

PROOST ET AL.

Examiner

Jessica H. Roark

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 23 May 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 5-8, 10, 11, 13 and 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 9 and 12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☒ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948).

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No.(s) 4

19) ☐ Notice of Informal Patent Application (PTO-111)

20) ☒ Other Notice to comply with Sequence Rules

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#### DETAILED ACTION

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jessica Roark, Art Unit 1644, Technology 1600.

2. Applicant's election with traverse of Group I (claims 1-4 and 9) in Paper No. 10 is acknowledged. The traversal is on the grounds that a search for Group III and IV can be carried out along with a search for Group I without undue burden.

This argument is found persuasive in part:

Group IV, drawn to a pharmaceutical composition comprising the protein will be rejoined with Group I.

However, this argument is not found persuasive with respect to Group III. As set forth in Paper No. 9, Groups I and III are distinct, since the protein can be used in a materially different process, and a search for Group I is not co-extensive with a search for Group III, as shown by their classification.

The requirement is still deemed proper with respect to Groups II, III and V, and is therefore made FINAL.

Claims 5-8, 10-11 and 13-14 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

*Claims 1-4, 9 and 12 are under consideration in the instant application.*

3. Sequence compliance: Applicant's provision of a CRF, Sequence Listing, and Statement that the contents are identical on 2/26/01 (Paper No. 6), is acknowledged. The CRF has been found acceptable and entered.

However, it is noted that SEQ ID NO:1 does not conform with 37 CFR 1.822 (d)(4) (see also MPEP 2422.02-2422.03) in that the numbering used does not reflect the fact that the mature protein begins with the sequence Ser-Pro-Tyr-Ser-Ser that currently corresponds to residues numbered 24-28 of SEQ ID NO:1. Numbering indicating the start of the mature protein is essential to the instant invention.

**Therefore, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth above and on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.**

**In addition,** Applicant is required to identify the nucleotide and amino acid sequences with SEQ. ID NOS wherever sequences occur in the specification and drawings (*at least in the "Brief Description", e.g. for Figure 1*), in order to satisfy the requirements of 37 CFR 1.821 (d) (see also MPEP 2422.02-2422.03). In particular, it is noted that the RANTES sequences presented in Figure 1 requires reference to the corresponding SEQ ID NO: 6 i.e. SEQ ID NO:1 AFTER Applicant has complied with 37 CFR 1.822(d)(4)).

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4. Acknowledgment is made of applicant's claim for foreign priority based on application 97116863.8 filed in Europe on 9/29/97; application 97122471.2 filed in Europe on 12/19/97; and application 98104216.1 filed in Europe on 3/10/98. It is noted, however, that applicant has not filed certified copies of these applications as required by 35 U.S.C. 119(b). Therefore, intervening references have been applied under 35 USC 102(a).

5. Applicant's IDS, filed 8/22/00 (Paper No. 4), is acknowledged.

6. Formal drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

7. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

8. Claims 1 and 2 are objected to under 37CFR 1.821(d) for failing to recite the SEQ ID NOS. in the claims.

9. Claim 4 is objected to under 37 CFR § 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only. See MPEP § 608.01(n). Even though this claim is in improper form, the examiner has chosen to examine the claim.

10. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.

11. Claims 9 and 12 are objected to under 37 CFR § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim (e.g., claim 4). See MPEP § 608.01(n). Even though these claims are in improper form, the examiner has chosen to examine claims.

12. 35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any

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13. Claims 1-4 and 9 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter, a product of nature.

The instant claims are drawn to an amino-terminally truncated RANTES, lacking amino acids 1-2. The specification discloses on page 12 at lines 3-18 that RANTES lacking amino acids 1-2 compared to "intact" RANTES is the form of RANTES produced by cells.

The amino-terminally truncated RANTES as claimed has the same characteristics and utility as found naturally in RANTES produced by various cells, and therefore does not constitute statutory subject matter. Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980). Mere purity of a naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). See also American Wood v. Fiber Disintegrating Co., 90 U.S. 566 (1974); American Fruit Growers v. Brogdex Co., 283 U.S. 1 (1931); Funk Brothers Seed Co. v. Kalo Inoculant Co., U.S. 127 (1948).

It is suggested that Applicant amend the claims to recite that a "purified" protein, as disclosed on page 5 at lines 22-31.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

14. The following is a quotation of the second paragraph of 35 U.S.C. 112.

*The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

15. Claims 1-2, 4, 9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-2, 4, 9 and 12 are indefinite in the recitation of "residues 1, 1-2, 1-3 or 1-4 of the naturally occurring RANTES" and "residues 1-2 of the naturally occurring RANTES". In the absence of SEQ ID NOS, both the numbering and identity of the amino acids is ambiguous and renders the metes and bounds of the phrases unclear. It is suggested that Applicant amend the claims to recite a reference SEQ ID NO:1 AFTER correction as per Section 3.

B) Claims 1-2, 4, 9 and 12 are ambiguous in the recitation of "lacking ... residues 1, 1-2, 1-3 or 1-4" and "lacking residues 1-2". As currently recited the meaning of these phrases is unclear. For example, the claims can be interpreted to be drawn to any protein lacking these residues, regardless of whether or not additional residues are also missing. Alternatively, the claims can be interpreted to be drawn to a protein lacking ONLY either residue 1, residues 1-2, etc. It is suggested that Applicant amend the claim to clearly set forth the limitations of the claim, for example by reciting an amino-terminally truncated RANTES consisting of (renumbered as per (A)) SEQ ID NO:1 from (e.g.) 1-68.

C) Claims 1-4, 9 and 12 are indefinite in the recitation of "naturally occurring". The specification does not appear to provide a clear definition of this term. Further, the specification indicates on page 12 at lines 13-16 that the form of RANTES lacking residues 1 and 2 compared to "intact" RANTES is

1. The term "naturally occurring" is ambiguous as currently

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D) Claims 9 and 12 recite the limitation "protein according to any of the claims from 1 to 4" in the preamble. There is insufficient antecedent basis for this limitation in the claim.

E) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.0.

16. For examination purposes under 35 USC 102 and 103, the reference sequence for RANTES is considered to be that of instant Figure 1, where amino acid residues #1-4 are Ser-Pro-Tyr-Ser.

In addition, and as noted supra, claims not limited by a SEQ ID NO: are considered to encompass any RANTES protein lacking the amino acids of the numbered positions, including more extensive truncations of RANTES which lack not only those amino acid residues recited, but also additional residues.

Finally, "naturally-occurring RANTES" is interpreted to be RANTES consisting of amino acids 1-68, as presented in Figure 1.

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.*

*(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

*(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.*

18. Claims 1-3, 9 and 12 are rejected under 35 U.S.C. 102(a) as being anticipated by Oravecz et al (J. Exp. Med. 1997;186:1865-1872, IDS AT; see entire document).

Oravecz et al. teach an amino-terminally truncated RANTES, lacking amino acids corresponding to amino acid residues 1-2 of the amino acids sequences of the full length RANTES of instant Figure 1, which is SEQ ID NO.2 (see entire document, e.g., Abstract). Oravecz et al. also teach that RANTES lacking amino-terminal amino acids 1-2 is a potent antagonist of HIV-1 (e.g. bridging paragraph of pages 1869-1870, and Figure 7). In addition, although truncated RANTES in a pharmaceutically acceptable carrier is not explicitly taught, such a carrier is inherently present in the formulations of the protein used in the cell culture experiment of Figure 7.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein. In addition, Applicant is reminded that intended uses do not carry patentable weight per se, and the claim

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19. Claims 1-4 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Noso et al. (J. Immunol. 1996;156:1946-1953, see entire document).

Noso et al. teach an amino-terminally truncated RANTES consisting of 66 amino acids and derived from dermal fibroblasts (see entire document, e.g. page 1948 2<sup>nd</sup> column, especially 5<sup>th</sup> paragraph, and Figure 3). The amino acid sequence of SEQ ID NO:2 would be an inherent property of the RANTES taught by Noso et al. since Figure 3 indicates that it is the amino acids corresponding to positions 1 and 2 that are missing from the 68 amino acid form of RANTES. In addition, Noso et al. teach glycosylated species of this truncated form of RANTES (e.g. page 1948, 2<sup>nd</sup> column, especially 5<sup>th</sup> paragraph).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein. In addition, Applicant is reminded that intended uses do not carry patentable weight per se, and the claim reads on the active or essential ingredients.

20. Claims 1-2, 9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Gong et al. (J. Biol. Chem. 1996;271:10521-10527, IDS AO: see entire document).

Gong et al. teach amino-terminally truncated RANTES lacking NH<sub>2</sub>-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3, or 1-4; and having chemokine antagonistic activity (see entire document, especially Figure 1 and Table I). As noted supra in sections 15 and 16, instant claims 1 and 2 are not limited to truncations involving ONLY amino acids 1 or 1-2, 1-3 or 1-4. In addition, although truncated RANTES in a pharmaceutically acceptable carrier is not explicitly taught, such a carrier is inherently present in the formulations of the protein used in the cell culture experiments of Figures 2-4.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein. In addition, Applicant is reminded that intended uses do not carry patentable weight per se, and the claim reads on the active or essential ingredients.

21. Claims 1-2, 4, 9 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Rollins et al. (US Pat. No. 5,739,103, see entire document).

Rollins et al. teach and claim an amino-terminally truncated RANTES having antagonistic activity, and methods comprising administering the amino-terminally truncated RANTES (see entire document, especially columns 3 and 6-8 as well as the claims). The amino-terminally truncated RANTES taught by Rollins et al. include truncation of at least amino acids 1 and 2, since column 3 (as well as claims 5-5-7) teach that the truncation is to be "about 1 to about 10 or about 2 to about 7". It is noted that instant claims 1 and 2 are not limited to truncations involving ONLY amino acids 1 or 1-2, 1-3 or 1-4.

In addition, Rollins et al. teach recombinant production of amino-terminally truncated chemokines in eukaryotic cells, which would inherently result in a glycosylated protein (e.g., column 8, especially lines 11-20). Finally, Rollins et al. teach the formulation of the amino-terminally truncated RANTES in a

pharmaceutically acceptable carrier for treatment of a RANTES-mediated

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Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced protein. In addition, Applicant is reminded that intended uses do not carry patentable weight per se, and the claim reads on the active or essential ingredients.

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

*(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

23. Claims 1-4, 9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gong et al. (J. Biol. Chem 1996;271:10521-10527, IDS AO).

The claims are drawn to amino-terminally truncated RANTES, lacking NH<sub>2</sub>-terminal amino acids corresponding to amino acid residues 1, 1-2, 1-3, or 1-4 and having antagonistic activity, and a pharmaceutical composition thereof.

Gong et al. have been discussed supra and teach amino-terminally truncated RANTES lacking amino acids 1, 1-2, 1-3, and 1-4; and having antagonistic activity.

Gong et al. differ by not teaching an amino-terminally truncated RANTES having the amino acid sequence of SEQ ID NO:2 and by not explicitly teaching a pharmaceutical composition comprising the amino-terminally truncated RANTES.

However, Gong et al. also teach that the functional activity of RANTES is encoded in amino acids 1-5, since various truncations which included amino acids 1-5 resulted in forms of RANTES that lacked functional activity (e.g., page 10523, "Functional Activity of Shortened Analogs"). In addition, Gong et al. teach that truncations of RANTES involving amino acid residues 1-7, 1-8, 1-9 and 1-10 results in binding by these truncated forms of RANTES to receptors not normally bound by full length RANTES (e.g., page bridging paragraph of pages 10524 and 10525), causing Gong et al. to conclude that the specificity of RANTES lay within residues 1-6 (e.g., page 10525 last paragraph). Gong et al. teach screening of the various truncation in several assays which permit determination of whether a truncated form of RANTES is an antagonist, and how efficiently that particular truncation functions as an



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Therefore, the ordinary artisan at the time the invention was made would have been motivated to provide additional truncations of RANTES, including SEQ ID NO:2, by focusing on residues 1-6 of the amino terminal in order to identify truncated forms of RANTES that were antagonistic for RANTES, but that did not cross inhibit interactions of other chemokines with their receptors. Given the teachings of Gong et al. that functional activity requires residues 1-5, the ordinary artisan would have been further motivated to produce and screen truncations of RANTES lacking amino terminal residues 1, 1-2, 1-3, and 1-4. In addition, given the teachings of Gong et al. that multiple amino terminal truncations of RANTES result in forms of RANTES having chemokine antagonistic activity and the teachings of assays for assessing antagonistic activity, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success in producing the claimed invention, including SEQ ID NO:2, as a matter of routine optimization. Further, the ordinary artisan would have been motivated to provide pharmaceutical compositions comprising any such antagonists in order to evaluate their relative efficacy in various disease models of inflammation, as taught by Gong et al.; and would have had a reasonable expectation of successfully utilizing these RANTES antagonistic pharmaceutical compositions in inhibiting at least some models of inflammation. Finally, glycosylated forms of the amino-terminally truncated RANTES antagonistic proteins would be produced as a consequence of many different expression systems that the ordinary artisan would utilize in order to produce sufficient quantities of the truncated RANTES. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

24. No claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.

PHILIP GAMBEI PH.D.

## Notice to Comply

Application No.

09/537,858

Examiner

Jessica H. Roark

Applicant(s)

PROOST ET AL.

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### NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: Please see Section 3 of attached Office Action.

#### Applicant Must Provide:

- ☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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